Epigenetic regulation of planarian stem cells by the SET1/MLL family of histone methyltransferases.

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Authors: Amy Hubert, Jordana M Henderson, Kelly G Ross, Martis W Cowles, Jessica Torres, Ricardo M Zayas

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Public Summary:
The role of chromatin regulation in stem cells was studied in vivo by looking at regeneration in the freshwater planarian Schmidtea mediterranea. These animals possess a high concentration of pluripotent stem cells, which are capable of restoring any damaged or lost tissues after injury or amputation. We identified S. mediterranea homologs of the SET1/MLL family of histone methyltransferases and COMPASS and COMPASS-like complex proteins and investigated their role in stem cell function during regeneration. With this work, we characterize the function of the SET1/MLL family in the context of planarian regeneration and gain insight into the role of these enzymes in adult stem cell regulation in vivo. (Adapted from Epigenetics 8:1, 1–2).

Scientific Abstract:
Chromatin regulation is a fundamental mechanism underlying stem cell pluripotency, differentiation, and the establishment of cell type-specific gene expression profiles. To examine the role of chromatin regulation in stem cells in vivo, we study regeneration in the freshwater planarian Schmidtea mediterranea. These animals possess a high concentration of pluripotent stem cells, which are capable of restoring any damaged or lost tissues after injury or amputation. Here, we identify the S. mediterranea homologs of the SET1/MLL family of histone methyltransferases and COMPASS and COMPASS-like complex proteins and investigate their role in stem cell function during regeneration. We identified six S. mediterranea homologs of the SET1/MLL family (set1, mll1/2, trr-1, trr-2, mll5-1 and mll5-2), characterized their patterns of expression in the animal, and examined their function by RNAi. All members of this family are expressed in the stem cell population and differentiated tissues. We show that set1, mll1/2, trr-1, and mll5-2 are required for regeneration and that set1, trr-1 and mll5-2 play roles in the regulation of mitosis. Most notably, knockdown of the planarian set1 homolog leads to stem cell depletion. A subset of planarian homologs of COMPASS and COMPASS-like complex proteins are also expressed in stem cells and implicated in regeneration, but the knockdown phenotypes suggest that some complex members also function in other aspects of planarian biology. This work characterizes the function of the SET1/MLL family in the context of planarian regeneration and provides insight into the role of these enzymes in adult stem cell regulation in vivo.